Resolving Intertracer Inconsistencies in Soil Ingestion Estimation

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In this article we explore sources and magnitude of positive and negative error in soil ingestion estimates for children on a subject-week and trace element basis. Errors varied among trace elements. Yttrium and zirconium displayed predominantly negative error; titanium and vanadium usually displayed positive error. These factors lead to underestimation of soil ingestion estimates by yttrium and zirconium and a large overestimation by vanadium. The most reliable tracers for soil ingestion estimates were aluminum, silicon, and yttrium. However, the most reliable trace element for a specific subject-day (or week) would be the element with the least error during that time period. The present analysis replaces our previous recommendations that zirconium and titanium are the most reliable trace elements in estimating soil ingestion by children. This report identifies limitations in applying the biostatistical model based on data for adults to data for children. The adult-based model used data less susceptible to negative bias and more susceptible to source error (positive bias) for titanium and vanadium than the data for children. These factors contributed significantly to inconsistencies in model predictions of soil ingestion rates for children. Correction for error at the subject-day level provides a foundation for generation of subject-specific daily soil ingestion distributions and for linking behavior to soil ingestion. *Key words*: dioxin, exposure assessment, risk assessment, soil ingestion. *Environ Health Perspect* 103:454–457 (1995)

Quantifying how much soil humans ingest became a major concern in the 1980s when soil ingestion estimates were needed to assess potential risk from sites contaminated by chemicals and radiation. The initial focus on the role of soil ingestion in health risk centered on dioxin contamination at Times Beach, Missouri; now soil ingestion estimates are routinely incorporated into all risk assessment procedures for contaminated sites (*1*). To aid in estimating soil ingestion, EPA has proposed daily soil ingestion rates for children and adults (*2*). Based on the nature of the contaminated site, estimated soil consumption has often been identified as one of the most significant routes of exposure affecting final risk assessment estimates (*1*).

The database on soil ingestion in humans is limited to five studies in children (*3*–*7*) and one study in adults (*8*). These studies used soil trace-element ("tracer") methodologies to estimate soil ingestion. The strengths and limitations of these studies and their capacity to provide defensible soil ingestion estimates have been assessed (*9*).

Of particular concern is that the soil ingestion studies demonstrated relatively poor intertracer consistency within a single study. As Table 1 indicates, the range of soil ingestion estimates can vary considerably among the tracers within each study. For example, in the Calabrese et al. (*5*) study, the median tracer-based soil ingestion values ranged from 9 to 96 mg/day, the mean from 21 to 459 mg/day, and the upper 95% boundary from 106 to 2100 mg/day, depending on the tracer used. Such divergent estimates could have any number of effects on the risk assessment process. A key problem has been determining which tracers provide the best estimates. The present study offers a quantitative solution to this problem of selecting tracers. We identify the principal sources of positive and negative error in mass-balance soil ingestion studies and quantify and correct the error by subject-day for each tracer. These adjustments are presented for the Calabrese et al. (*5*) report since this mass-balance study provided daily measurements of collected samples. The only other mass-balance soil ingestion study, which was published by Davis et al. (*7*), could not be corrected for positive and negative error using the developed methods because daily measurements were not taken and only three tracers were measured.

Choosing the Best Tracer

We previously conducted an "adult validation study" (*5*) using the same methods as the study in children. This validation study involved ingestion of known amounts of soil (100, 500 mg/day) by adult volunteers. Our purpose was to assess whether the study protocol could detect and precisely quantify soil ingestion in subjects when modest (100 mg/day) to substantial (500 mg/day) amounts of soil were ingested daily. In the adult validation study, the tracers that displayed close to 100% recovery were aluminum, silicon, yttrium, and zirconium. These elements were considered to be the most reliable tracers in the children's study (*5*). We initially assumed that tracers performing well in the adult tracer recovery study would also perform well in the children's soil ingestion study. Later we found that this assumption was unreliable (*9*): recovery is essentially a mathematical function of the amount of trace elements consumed in food compared to the amount ingested in soil. Tracers with low food-to-soil (F/S) ratios displayed better recovery. We developed a model to estimate the soil ingestion detection of tracers for varying sample sizes based on this concept (*10*).

Of particular interest was the large difference in F/S ratios for some tracers between children and adults. For example, the F/S ratio for titanium was nearly 10-fold lower in children than it was in adults (*9*). This suggested that even though titanium performed quite poorly in the adult tracer recovery study, it most likely had excellent recovery in the children's soil ingestion study. In fact, when applied to children's soil ingestion data, the soil ingestion detection model predicted that only two tracers (titanium, zirconium) displayed an acceptable estimated precision of recovery (100% ± 20%). These findings therefore led us to reject the original assumption that the most reliable tracers for the adult recovery studies would be the most reliable in the children's study.

However, there were still unresolved inconsistencies in estimates for titanium and zirconium. For example, if zirconium was such a reliable tracer in the children's study, why did it lead to highly inconsistent soil ingestion estimates for the one child that exhibited soil pica (*5*)? The soil ingestion estimates for this child for all tracers except zirconium were 5–6.5 g/day over a 2-week period, whereas the estimate based on zirconium, was 1.5 g/day for the same period. To have one of the two "best" tracers apparently underestimate the soil ingestion by 75% was troubling. The underestimation of soil ingestion by zirconium for the child exhibiting pica seemed to mirror the soil ingestion estimates for the entire sample, in which the median value for zirconium was about 70% less than that of titanium. How could the two "best" tracers differ substantially in the median (16 versus 55 mg/day), mean (25 versus 218 mg/day), and upper 95% (106 versus 1492 mg/day)? Questions were also raised about the reliability of the zirconium estimates, and an important source of error for titanium was determined, indicating that both children and adults most likely ingested quantities of titanium that were neither in food nor soil but from a different, unknown source that contributed to overestimates of soil ingestion in affected subjects (*11*). Such observations led us to rethink the question of which tracers provided the most reliable estimates of soil ingestion, with particular emphasis on understanding the basis for intertracer variability in estimating soil ingestion.

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One of the basic assumptions inherent in interpreting mass-balance soil ingestion studies is that positive and negative error will likely occur as a result of flaws in the study design. However, we assumed initially that the capacity for positive error would approximate negative error and they would cancel other out with respect to subject average values (*5*). In fact, negative soil ingestion values, which comprised 12–44% of soil ingestion estimates depending on the tracer in the children's study (*5*) was attributted to negative error, as it is not possible to have negative soil ingestion. However, we believed that positive error would also exist that would presumably offset the negative error. This assumption was never deeply explored in any of our original soil ingestion study reports. However, as we will show, this assumption appears to be of limited validity and leads to significant implications depending on the tracer.

We first provide a general framework for classifying various sources of error for soil ingestion. We follow this discussion with a description of a methodology for quantifying these sources. Finally, we present estimates based on implementing this methodology in our children's study (*5*).

Causes of Error

In mass-balance soil ingestion studies, positive and negative error are the result of a variety of causes. For example, if tracers are ingested in food but are not captured in the fecal sample as a result of either a slow transit time or because a fecal sample was not available for the final day(s) of the study, the soil ingestion estimate will have a negative bias. In addition, sample measurement errors, resulting in diminished detection of fecal tracers but not soil tracer levels, will negatively bias soil ingestion estimates.

Ingestion of high levels of tracers in the days before the study starts and low ingestion during the study could result in an overestimation of soil ingestion. Positive error can also occur if the subject ingests tracers from a source that is of neither soil nor food origin during the study period. For example, if a child eats a piece of paper that contains titanium in the printing material, this could lead to an overestimation of soil ingestion based on this particular tracer. If tracer was measured incorrectly in soil but not in the fecal sample, this could also result in positive error. Negative and positive error can be quantified for a single day or totaled for a subject-week.

In a previous paper (*12*), we reported that the quantification of negative and positive error led to improved daily soil ingestion estimates. In our previous reports, daily soil ingestion estimates were obtained by dividing the total soil ingestion observed by the number of days of study (e.g., 3–8) and not based on a particular day.

Quantifying Error

Obtaining the best estimate of soil ingestion for a given subject-day. To determine positive or negative error in soil ingestion estimates, it is necessary to develop a procedure for obtaining an unbiased estimate of soil ingestion. In the absence of direct knowledge of actual soil ingestion, the approach adopted in the present analysis was to: 1) Incorporate an assumed GI tract transit time of 28 hr for the passage of tracers ingested in food to the feces. This value was applied to all subject-day estimates. Inter- and intraindividual variation in GI transit time was not considered. 2) Estimate the daily soil ingestion rate for each tracer for each 24-hr day for which a fecal sample was obtained. We assume that the corresponding food ingestion period is a 24-hr period beginning 28 hr earlier than the start of the fecal sample period. 3) Determine the median tracer-based soil ingestion rate for each subject-day. Upper and lower bounds for the range of estimates were determined based on criteria formed using an assumption of the magnitude of the relative standard deviation as described elsewhere (*12*). Daily soil ingestion estimates falling outside of these upper and lower boundaries were assumed to be unreliable and were excluded from subsequent calculations. The median of the remaining tracer elements of the daily soil ingestion rates was deemed the best estimate of soil ingestion for the particular day. Tracers found to be unreliable displayed either positive or negative error depending on whether the tracer exceeded the upper or lower boundary. The magnitude of positive or negative error for a specific tracer for a day was then obtained by determining the difference between the value for the tracer and the median value. 4) Determine negative error due to missing fecal samples at the end of the study period. In the children's study (*5*), we estimated soil ingestion by developing an average daily tracer ingestion rate from food over 3 days. This average daily food tracer intake was subtracted from the average daily fecal tracer levels over the 4 days of fecal collection. The principal problem with this approach was that for 43 of 128 subject-weeks, there was no fecal sample for day 4 of the study. This would lead to an underestimation of soil ingestion (i.e., negative error). The situation became even more extreme for a smaller number of subjects for which no fecal samples were provided on days 3 and 4 (five subject-weeks) and on days 2, 3, and 4 (two subject-weeks). As expected, the likelihood of negative soil ingestion estimates for subjects with missing last-day fecal samples was markedly enhanced. In this case, negative error would have been minimized if the daily tracer intake from food were low or maximized if the daily tracer intake from food were high and transit time was sufficiently slow to prevent capture in the fecal sample. Thus, even though a day 4 fecal sample was not available, this would not directly lead to a large negative error, nor would availability of day 4 fecal sample automatically preclude this type of negative error. This reasoning is consistent with the observation (*9,10*) that a low F/S ratio was an important predictor of tracer recovery in the adult validation procedure.

Table 2 indicates the estimated magnitude of positive and negative error for six tracers in the children's study (*5*). The original mean soil ingestion estimates ranged from a low of 21 mg/day based on zirconium to a high of 459 mg/day based on vanadium. After correcting for positive and negative error, the range in soil ingestion estimates decreased to 97 mg/day based on yttrium to 208 mg/day based on titanium. This represents a change in the range from approximately 21-fold to approximately 2-fold. With the exclusion of titanium and vanadium, which were most susceptible to error, the range of the remaining four corrected tracers is from 97 to 136 mg/day. Consequently, correction for positive and negative error resulted in considerable intertracer agreement for esti-

Table 1. Soil ingestion estimates in children (mg/day)

	Binder et al. (*3*)		Van Wijnen et al. (*6*)		Davis et al. (*7*)		Calabrese et al. (*5*)	
Trace element	Mean	Median	Mean	Median	Mean	Median	Mean	Median
Aluminum	181	121			40	25	153	29
Silicon	184	136			82	59	154	40
Titanium	1834	618			246	81	218	55
Barium							32	<0
Manganese							<0	<0
Vanadium							459	96
Yttrium							85	9
Zirconium							21	16
Limiting tracer method								
Day-care center			103	111				
Campers			213	160				

Table 2. Positive/negative error (bias) in soil ingestion estimates in the Calabrese et al. (1989) mass-balance study (*5*): effect on mean soil ingestion estimate (mg/day)[a]

Trace element	Negative error: Lack of fecal sample on final study day	Negative error: Other causes[b]	Negative error: Total negative error	Total positive error	Net error	Original mean	Adjusted mean
Aluminum	14	11	25	43	+18	153	136
Silicon	15	6	21	41	+20	154	133
Titanium	82	187	269	282	+13	218	208
Vanadium	66	55	121	432	+311	459	148
Yttrium	8	26	34	22	-12	85	97
Zirconium	6	91	97	5	-92	21	113

[a]How to read table: for example, aluminum as a soil tracer displayed both negative and positive error. The cumulative total negative error is estimated to bias the mean estimate by 25 mg/day downward. However, aluminum has positive error biasing the original mean upward by 43 mg/day. The net bias in the original mean was 18 mg/day positive bias. Thus, the original 156 mg/day mean for aluminum should be corrected downward to 136 mg/day.
[b]Values indicate impact on mean of 128-subject-weeks in milligrams of soil ingested per day.

mation of soil ingestion rates. Table 2 indicates that each tracer displayed some degree of positive and negative error. However, there were marked differences among the tracers with respect to their susceptibility to error. Titanium and vanadium displayed exceptionally high positive and negative, error; zirconium also displayed a high amount of negative error. The negative error attributed to missing last-day fecal samples affected the estimates of soil ingestion for all tracers to some extent, but most notably for titanium and vanadium, where the original mean was negatively biased by 82 and 66 mg/day, respectively. Negative error attributed to all other principal causes of error (e.g., input/output misalignment, sample loss) was also highly variable, with titanium being most susceptible (187 mg/day) followed by zirconium (91 mg/day) and vanadium (55 mg/day). The most likely cause of this negative error for titanium and vanadium is input/output misalignment because the daily ingestion of these tracers in food was highly variable. Such variable daily tracer intakes, coupled with transit times longer than 28 hr for a given subject, could have led to negative error.

In the case of zirconium, negative error may be more complex than simply input/output misalignment. Based on the pattern of negative soil ingestion estimates, the modest variability of zirconium in the diet (*13*), and the recognized difficulty of analyzing zirconium (*14*), we hypothesize that a substantial component of the 91 mg/day is attributed to sample measurement loss of fecal tracer levels.

Positive error was highest for vanadium (432 mg/day), followed by titanium (282 mg/day). The remaining four tracers displayed positive error <50 mg/day. The two principal causes of positive error are input/output misalignment and source error. Positive misalignment error would occur as a consequence of previous negative misalignment error. For example, if a subject displayed negative misalignment on day 2, it is likely that positive misalignment would occur on a subsequent day, although this would depend on the transit time in relation to the end of the observation period. Second, consumption of tracers in a nonfood/nonsoil source will contribute to positive bias. For example, subject 833 displayed low (<100 mg/day) soil ingestion for all tracers except vanadium (11 g/day) during week 2. This subject ingested about 10–15 µg/day vanadium in food. However, on day 4 of week 2, this subject excreted nearly 5000 µg vanadium in feces. This vanadium could not have come from food or soil. If so, other tracers would have indicated similarly high soil ingestion estimates. Thus, the high level of vanadium in feces came from an unknown source. This type of source-error was particularly apparent for titanium and vanadium.

Discussion

The present analysis identifies and quantifies element-specific sources of error in our children's study (*5*) that led to widely varying tracer-specific estimates. Correcting for such error at the individual level for each tracer provides substantially more reliable estimates of soil ingestion. The methodology leads to corrected soil ingestion estimates that provide similar mean estimates of soil ingestion across all tracers (Table 2). The range of mean tracer-based soil ingestion estimates for the six tracers has narrowed from 21 to 459 mg/day to 97 to 208 mg/day. This represents a marked improvement in estimation.

Despite the substantial improvement in intertracer estimation of subject-week soil ingestion estimates, the analysis revealed a sound basis on which to select the most reliable tracers and the most reliable subject-day estimates. The tracers requiring the least amount of error correction for a subject-week or subject-day would be expected to provide the most reliable estimates for that time.

Our findings indicate that aluminum, silicon, and yttrium, which displayed the least net bias along with modest and nearly equal positive and negative error, are the most reliable tracers in the children's study (*5*). These findings differ from our earlier reports (*9,10*), in which we argued that the most reliable tracers in the children's soil ingestion study were titanium and zirconium. Why should the biomathematical model which predicted tracer recovery with a high degree of precision based on the F/S ratio yield a different result? We believe that two factors contributed to the difference in tracer selection. First, the biostatistical model was developed using data for adults and was then applied to children. While the F/S ratios may be appropriately replaced by ratios for children, the pattern of fecal samples differs markedly between adults and children. Adults had daily fecal samples for all days in the study, while 39% of the children did not report fecal samples for the last days in the study week. This type of output misalignment was not accounted for in the biostatistical model, but it was in the present report.

Second, the biostatistical model used only the F/S ratio to evaluate the adequacy of tracer-specific soil ingestion. Although variability in tracer intake was probably related to the accuracy of soil ingestion estimates, this was not accounted for in the biostatistical model. In contrast, variability in tracer intake via food would lead to large intertracer differences between soil ingestion estimates for a given subject-day. Determining the best estimate for a specific day eliminates such extreme estimates. For these reasons, we believe that the present analysis [with soil ingestion estimates given earlier (*12*)] is clearly superior to soil ingestion estimates based on the original biostatistical model.

It should be noted that other approaches could be used to quantify and correct for error both on a subject-week and subject-day basis. We have explored several such options, including different time assumptions and various approaches for deriving the best estimate for error quantification. Comparisons of these approaches led to basically similar final, corrected mean estimates.

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